RE: "DIETARY PATTERNS ASSOCIATED WITH A LOW-FAT DIET IN THE NATIONAL HEALTH EXAMINATION FOLLOW-UP STUDY: IDENTIFICATION OF POTENTIAL CONFOUNDERS FOR EPIDEMIOLOGIC ANALYSES" AND "TOWARD A CLEARER DEFINITION OF CONFOUNDING"

In a recent paper by Ursin et al. (1), some interesting analyses of correlations among selected dietary factors were performed. I believe that one of the authors' conclusions requires more thorough consideration, however. It was stated that intake of specific nutrients and food groups should be considered potential confounders in studies involving dietary fat intake as a risk factor for certain cancers. This is indeed logical given their results, but before investigators begin adjusting for certain other food group intakes in their analyses, the order of events should be considered. As the authors speculate, individuals who choose to eat low-fat diets substitute "certain carbohydrate rich foods such as fruits and vegetables for fat." Thus, intakes of fruits or of vegetables among low-fat diet consumers are at least partly the product of individuals' choices for the low-fat diets.

In another recent contribution, Weinberg (2) shows that control or adjustment of an effect estimate for a potentially confounding factor can lead to substantial bias in the effect estimate when the factor is at least partly caused by the exposure. The adjustment factor may even behave as an effect modifier in such analyses. Therefore, carbohydrate rich dietary intake factors should not be treated as potential confounders in the analysis of studies of effects of low-fat dietary intakes on certain cancers unless the concerns raised here are rigorously ruled out.

REFERENCES

1. Ursin G, Ziegler RG, Subar AF, et al. Dietary patterns associated with a low-fat diet in the National Health Examination Follow-up Study: identification of potential confounders for epidemiologic analyses. Am J Epidemiol 1993;137:916–27.
2. Weinberg CR. Toward a clearer definition of confounding. Am J Epidemiol 1993;137:1–8.

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URSIN ET AL. REPLY

We thank Dr. Scholl (1) for the opportunity to clarify a few issues. In our study of dietary patterns associated with a low-fat diet in the National Health Examination Follow-Up Study (NHEFS) (2), we avoided making statements about causality such as whether consuming a low-fat diet resulted from a high intake of fruits and vegetables, or whether high fruit and vegetable intake was a result of a low-fat diet. We think such directionality interpretations are difficult to make on the basis of cross-sectional dietary patterns. In our study, participants completed a food-frequency questionnaire designed to assess the usual intake of all major nutrients over the past 12 months. We examined associations between a low-fat diet and the concurrent intake of other nutrients and food groups over the same 12-month period. As long as both dietary factors estimated intake over the same time period, we do not think one can conclude that the low-fat diet "caused" the high fruit and vegetable intake.

In observational studies, dietary estimates from food-frequency questionnaires are often used as proxy estimates of the diet over a certain time period (such as the average diet 10 years prior to disease onset). Under these circumstances, one could possibly argue that the intake of one variable "caused" the other, i.e., that the low-fat diet caused a high fruit and vegetable intake, and the other way around. Thus, high fruit and vegetable intake could be both a confounder and an intermediate variable on the causal pathway between a low-fat diet and the disease of interest. In this case, traditional epidemiologic methods do not allow for unbiased adjustments of such variables (3–5). Assuming, however, that one is restricted to using traditional methods, then, if fruit and vegetable intake was a stronger determinant of consuming a diet low in fat than vice versa, i.e., fruit and vegetable intake was a stronger confounder than it was an intermediate variable, it might still be better to adjust than to not adjust for fruit and vegetable intake when examining the effect of a low-fat diet.

By adjusting for fruit and vegetable intake in this manner, we are investigating the effect of a low-fat diet independent of fruit and vegetable intake. However, as demonstrated by Robins and Greenland (3), this approach may not yield an unbiased estimate of the independent or "direct" effect of a low-fat diet. Furthermore, if the two dietary components are too highly correlated, a model with both of them included would not be able to separate out their independent effects. However, as we demonstrated in our paper, the correlations between percent of calories from fat and fruits and vegetables were not so high as to preclude assessment of independent effects (Pearson's correlation coeffi-

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cient was −0.08 for vegetables and −0.38 for fruits) (2). In other words, it is possible to have a diet low in percent of calories from fat without having a high fruit and vegetable intake; for example, by having a high grain intake.

A different question is addressed with a model containing dietary fat as the only dietary exposure. Then we are investigating the total impact of a low-fat dietary pattern, including the effects of the concurrent intake of fruits, vegetables, grains, red meat, and dairy products, etc., on the disease of interest. There are several ways to limit calories from fat, some of which may be positively and others negatively associated with the disease in question. Thus, this unadjusted effect estimate of a low-fat diet on the disease may be confounded in both directions. Although estimates such as this are sometimes used to indicate the overall public health impact of a low-fat diet in the population, these estimates may not be informative in elucidating disease etiology.

Often both of these analytic procedures are used in nutritional epidemiology research. An additional way to approach a situation when etiologic studies have implicated several partially correlated dietary factors as important risk factors for a disease is to identify a dietary pattern that integrates the different dietary factors believed to be important. One might, for instance, investigate the relative risk associated with a low fat/high fruit and vegetable/low red meat diet compared with a high fat/low fruit and vegetable/high red meat diet. This approach would, however, not be able to separate out the effect of fat independent of fruits, vegetables, and red meat.

In observational epidemiology, as well as in clinical trials, whenever two dietary patterns differ in terms of a single macronutrient, there must be other concurrent differences in the intake of calories or other macronutrients that may themselves influence the disease in question. This problem exists for all these models described. All the models referred to above may be useful, as long as the investigator is aware of what question each model addresses.

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DR. WEINBERG REPLIES

The letter by Scholl (1) cites my commentary on confounding (2) as a basis for criticizing the conclusions drawn by Ursin et al. (3). I had shown that adjustment for a factor (in my example, this was history of spontaneous abortion in a study of outcome of an index pregnancy) that had also been potentially caused in part by the exposure under study can cause dramatic bias in relative risk estimation or spurious evidence for effect modification. Scholl has applied this conceptual framework to studies of dietary components, and he seems to have concluded that because increased consumption of fruits and vegetables may be caused in part by lower fat consumption, consumption of fruits and vegetables should not be treated as a potential confounder in studies evaluating the etiologic role of fat consumption in cancer. While my own work was cited in support of this argument, if he is suggesting that risk models where fat intake is the exposure of interest should simply omit measures of consumption of fruits and vegetables, I do not agree.

There are qualitative differences among diets, which produce quantifiable and quite dramatic correlations among the measurable dietary components (3). The causal basis for such associa-